

WHAT IS CLAIMED IS:

1. A peptide comprising the following sequence:

Xaa₍₁₋₄₎CysXaa₍₆₎Xaa₍₇₎GlyXaa₍₉₎LeuXaa₍₁₁₎Xaa₍₁₂₎LeuCysXaa₍₁₅₎Xaa₍₁₆₎ Xaa₍₁₇₎
Xaa₍₁₈₎ (SEQ ID NO:1), wherein Xaa₍₁₋₄₎ is absent or is between 1 and
4 amino acids of any kind, Xaa₍₆₎, Xaa₍₇₎, Xaa₍₉₎, Xaa₍₁₁₎, Xaa₍₁₅₎, and
Xaa₍₁₆₎ are independently any amino acid, and Xaa₍₁₂₎, Xaa₍₁₇₎, and
Xaa₍₁₈₎ are independently Nal(1), His, Phe, Trp, Tyr, Pro, Gln, or
Met.

2. The peptide of claim 1 wherein Xaa₍₁₋₄₎, Xaa₍₆₎, Xaa₍₇₎, Xaa₍₉₎,
Xaa₍₁₁₎, Xaa₍₁₅₎, and Xaa₍₁₆₎ are independently Ala, Leu, Iso, Glu,
Arg, Val, Gly, Gln, Ser, Met, Pro, Thr, Asn, Lys, or Trp.

3. The peptide of claim 2 wherein Xaa₍₁₂₎, Xaa₍₁₇₎, and Xaa₍₁₈₎ are
independently Phe, Trp, Tyr, Pro, Gln, or Met.

4. The peptide of claim 1 wherein Xaa₍₁₋₄₎, Xaa₍₆₎, Xaa₍₇₎, Xaa₍₉₎,
Xaa₍₁₁₎, Xaa₍₁₅₎, and Xaa₍₁₆₎ are independently Ala, Glu, Arg, Val,
Gly, Gln, Ser, Pro, Asn, or Lys.

5. The peptide of claim 4 wherein Xaa₍₁₂₎, Xaa₍₁₇₎, and Xaa₍₁₈₎ are
independently Phe, Trp, or Tyr.

6. The peptide of claim 1 wherein Xaa₍₉₎ is Ala, Arg, Asn, or Pro.

7. The peptide of claim 1 wherein Xaa₍₉₎ is Pro.

- where

CysArgAlaGlyAsnLeuGlnTrpLeuCysGluLysTyrPhe (SEQ ID NO:6);
CysArgAlaGlyProLeuGlnTrpLeuCysGluLysTyrPhe, where the first Leu is
Nle (SEQ ID NO:7);
CysArgAlaGlyProLeuGlnTrpLeuCysGluLysTyrPhe, where the second Leu
is Nle (SEQ ID NO:8);
CysArgAlaGlyProLeuGlnArgLeuCysGluLysTyrPhe (SEQ ID NO:9);
CysArgAlaGlyProLeuGlnAlaLeuCysGluLysTyrPhe, where the second Ala
is Nal(1) (SEQ ID NO:10); or
CysArgAlaGlyProLeuGlnHisLeuCysGluLysTyrPhe (SEQ ID NO:11).

19. The peptide of claim 1 wherein C-terminal to the C-terminal
Xaa₍₁₈₎ is the sequence Xaa₍₁₉₎ThrTyr, wherein Xaa₍₁₉₎ is any amino
acid.

20. The peptide of claim 19 comprising the following sequence:
Xaa₍₁₋₄₎CysArgAlaGlyProLeuGlnTrpLeuCysGluXaa₍₁₆₎TyrPheXaa₍₁₉₎ThrTyr (SEQ
ID NO:12), wherein Xaa₍₁₆₎ is Lys or His and Xaa₍₁₉₎ is Ala, Ser, Gln,
Asp, Glu, or Lys.

21. The peptide of claim 19 comprising one of the following
sequences:

SerGluValGlyCysArgAlaGlyProLeuGlnTrpLeuCysGluLysTyrPheSerThrTyr
(SEQ ID NO:13);

SerGluValGlyCysArgAlaGlyProLeuGlnTrpLeuCysGluLysTyrPheAlaThrTyr
(SEQ ID NO:14);

SerGluValGlyCysArgAlaGlyProLeuGlnTrpLeuCysGluLysTyrPheGlnThrTyr
(SEQ ID NO:15);

SerGluValGlyCysArgAlaGlyProLeuGlnTrpLeuCysGluLysTyrPheGlnThrTyrThr
(SEQ ID NO:16);
SerGluValGlyCysArgAlaGlyProLeuGlnTrpLeuCysGluLysTyrPheAspThrTyr
(SEQ ID NO:17);
SerGluValGlyCysArgAlaGlyProLeuGlnTrpLeuCysGluLysTyrPheGluThrTyr
(SEQ ID NO:18);
SerGluValGlyCysArgAlaGlyProLeuGlnTrpLeuCysGluLysTyrPheLysThrTyr
(SEQ ID NO:19);
GluAlaArgValCysArgAlaGlyProLeuGlnTrpLeuCysGluLysTyrPheSerThrTyr
(SEQ ID NO:20);
GlyGlnGlnSerCysArgAlaGlyProLeuGlnTrpLeuCysGluLysTyrPheSerThrTyr
(SEQ ID NO:21);
AlaSerSerMetCysArgAlaGlyProLeuGlnTrpLeuCysGluLysTyrPheSerThrTyr
(SEQ ID NO:22);
GlnGlyProAspCysArgAlaGlyProLeuGlnTrpLeuCysGluLysTyrPheSerThrTyr
(SEQ ID NO:23);
GlnAlaSerGluCysArgAlaGlyProLeuGlnTrpLeuCysGluLysTyrPheSerThrTyr
(SEQ ID NO:24);
AlaGluThrLeuCysArgAlaGlyProLeuGlnTrpLeuCysGluLysTyrPheSerThrTyr
(SEQ ID NO:25);
AsnSerLeuLeuCysArgAlaGlyProLeuGlnTrpLeuCysGluLysTyrPheSerThrTyr
(SEQ ID NO:26);
AlaGlnTrpValCysArgAlaGlyProLeuGlnTrpLeuCysGluLysTyrPheSerThrTyr
(SEQ ID NO:27);
GlyGlnGlnSerCysAlaAlaGlyProLeuGlnTrpLeuCysGluHisTyrPheSerThrTyr
(SEQ ID NO:28); or
GlyGlnGlnSerCysAlaAlaGlyProLeuGlnTrpLeuCysGluHisTyrPheSerThrTyr

22. The peptide of claim 19 wherein Xaa₍₁₉₎ is Ser.

GluAlaArgValCysArgAlaGlyProLeuGlnTrpLeuCysGluLysTyrPheSerThrTyr
(SEQ ID NO:20);

GlyGlnGlnSerCysAlaAlaGlyProLeuGlnTrpLeuCysGluHisTyrPheSerThrTyr
GlyArg (SEQ ID NO:29).

CysArgAlaGlyAlaLeuGlnTrpLeuCysGluLysTyrPhe (SEQ ID NO:4);

CysArgAlaGlyArgLeuGlnTrpLeuCysGluLysTyrPhe (SEQ ID NO:5);

CysArgAlaGlyAsnLeuGlnTrpLeuCysGluLysTyrPhe (SEQ ID NO:6);

CysArgAlaGlyProLeuGlnTrpLeuCysGluLysTyrPhe, where the first Leu is Nle (SEQ ID NO:7);

CysArgAlaGlyProLeuGlnTrpLeuCysGluLysTyrPhe, where the second Leu is Nle (SEQ ID NO:8);

CysArgAlaGlyProLeuGlnArgLeuCysGluLysTyrPhe (SEQ ID NO:9);

CysArgAlaGlyProLeuGlnAlaLeuCysGluLysTyrPhe, where the second Ala is Nal(1) (SEQ ID NO:10);

CysArgAlaGlyProLeuGlnHisLeuCysGluLysTyrPhe (SEQ ID NO:11);

SerGluValGlyCysArgAlaGlyProLeuGlnTrpLeuCysGluLysTyrPheAlaThrTyr
(SEO ID NO:14);

SerGluValGlyCysArgAlaGlyProLeuGlnTrpLeuCysGluLysTyrPheGlnThrTyr
(SEQ ID NO:15);

SerGluValGlyCysArgAlaGlyProLeuGlnTrpLeuCysGluLysTyrPheGlnThrTyrThr
(SEQ ID NO:16);

SerGluValGlyCysArgAlaGlyProLeuGlnTrpLeuCysGluLysTyrPheAspThrTyr
(SEQ ID NO:17);

SerGluValGlyCysArgAlaGlyProLeuGlnTrpLeuCysGluLysTyrPheGluThrTyr
(SEQ ID NO:18);

SerGluValGlyCysArgAlaGlyProLeuGlnTrpLeuCysGluLysTyrPheLysThrTyr
(SEQ ID NO:19);

GluAlaArgValCysArgAlaGlyProLeuGlnTrpLeuCysGluLysTyrPheSerThrTyr
(SEQ ID NO:20);

GlyGlnGlnSerCysArgAlaGlyProLeuGlnTrpLeuCysGluLysTyrPheSerThrTyr
(SEQ ID NO:21);

AlaSerSerMetCysArgAlaGlyProLeuGlnTrpLeuCysGluLysTyrPheSerThrTyr
(SEQ ID NO:22);

GlnGlyProAspCysArgAlaGlyProLeuGlnTrpLeuCysGluLysTyrPheSerThrTyr
(SEQ ID NO:23);

GlnAlaSerGluCysArgAlaGlyProLeuGlnTrpLeuCysGluLysTyrPheSerThrTyr
(SEQ ID NO:24);

AlaGluThrLeuCysArgAlaGlyProLeuGlnTrpLeuCysGluLysTyrPheSerThrTyr
(SEQ ID NO:25);

AsnSerLeuLeuCysArgAlaGlyProLeuGlnTrpLeuCysGluLysTyrPheSerThrTyr
(SEQ ID NO:26);

AlaGlnTrpValCysArgAlaGlyProLeuGlnTrpLeuCysGluLysTyrPheSerThrTyr
(SEQ ID NO:27);

GlyGlnGlnSerCysAlaAlaGlyProLeuGlnTrpLeuCysGluHisTyrPheSerThrTyr

(SEQ ID NO:28); or

GlyGlnGlnSerCysAlaAlaGlyProLeuGlnTrpLeuCysGluHisTyrPheSerThrTyr
GlyArg (SEQ ID NO:29).

25. The peptide of claim 1 that has a C-terminal fusion comprising the following sequence:

GlyGlyGlySerGlyGlyAlaGlnHisAspGluAlaValAspAsnLysPheAsnLysGlu
GlnGlnAsnAlaPheTyrGluIsoLeuHisLeuProAsnLeuAsnGluGluGlnArgAsnAla
PheIsoGlnSerLeuLysAspAspProSerGlnSerAlaAsnLeuLeuAlaGluAlaLysLys
LeuAsnAsp

AlaGlnAlaProAsnValAspMetAsn (SEQ ID NO:30).

26. The peptide of claim 19 that has a C-terminal fusion comprising the following sequence:

GlyGlyGlySerGlyGlyAlaGlnHisAspGluAlaValAspAsnLysPheAsnLysGlu
GlnGlnAsnAlaPheTyrGluIsoLeuHisLeuProAsnLeuAsnGluGluGlnArgAsnAla
PheIsoGlnSerLeuLysAspAspProSerGlnSerAlaAsnLeuLeuAlaGluAlaLysLys
LeuAsnAsp

AlaGlnAlaProAsnValAspMetAsn (SEQ ID NO:30).

27. A constrained helical peptide comprising a sequence of nine amino acid residues having a first terminal residue and a second terminal residue, wherein said residues flank an internal sequence of seven amino acids and have side-chains covalently bonded to each other to form a locking moiety and thereby constrain the peptide.

28. The peptide of claim 27 wherein the internal sequence is Xaa₍₇₎LeuAlaXaa₍₁₀₎Xaa₍₁₁₎Xaa₍₁₂₎Xaa₍₁₃₎ (SEQ ID NO:31), wherein Xaa₍₇₎, Xaa₍₁₁₎, Xaa₍₁₂₎, and Xaa₍₁₃₎ are independently Nal(1), His, Phe, Trp, Tyr, Pro, Gln, or Met, and Xaa₍₁₀₎ is any amino acid.

29. The peptide of claim 28 wherein the first and second terminal residues are independently Asp or Glu residues.

30. The peptide of claim 29 wherein the first and second terminal residues are Glu residues.

31. A peptide comprising the following sequence:

Xaa₍₁₋₄₎Xaa₍₅₎Xaa₍₆₋₇₎ProLeuGluXaa₍₁₁₎LeuAlaXaa₍₁₄₎Xaa₍₁₅₎Xaa₍₁₆₎Xaa₍₁₇₎GluXaa₍₁₉₎ (SEQ ID NO:32), wherein Xaa₍₁₋₄₎ is absent or is between 1 and 4 amino acids of any kind; Xaa₍₅₎ is any amino acid, Xaa₍₆₋₇₎ is absent or is between 1 and 2 amino acids, Xaa₍₁₄₎ and Xaa₍₁₅₎ are independently any amino acid, Xaa₍₁₁₎ and Xaa₍₁₆₎ are independently Nal(1), His, Phe, Trp, Tyr, Pro, Gln, or Met, Xaa₍₁₇₎ is absent or is 1-naphthyl-Ala, His, Phe, Trp, Tyr, Pro, Gln, or Met, and Xaa₍₁₉₎ is absent or is Gly.

32. The peptide of claim 31 wherein Xaa₍₁₋₄₎ is absent and an acetyl group is attached to Xaa₍₅₎.

33. The peptide of claim 31 wherein the Glu residues in SEQ ID NO:32 are joined by forming amides with 1,5-diaminopentane.

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34. The peptide of claim 31 wherein C-terminal to the C-terminal Xaa₍₁₉₎ is the sequence Xaa₍₂₀₎ThrTyr, wherein Xaa₍₂₀₎ is any amino acid.
35. The peptide of claim 34 wherein Xaa₍₂₀₎ is Ala, Ser, Gln, Asp, Glu, or Lys.
36. The peptide of claim 31 comprising the following sequence: Xaa₍₅₎Xaa₍₆₋₇₎ProLeuGluXaa₍₁₁₎LeuAlaXaa₍₁₄₎Xaa₍₁₅₎Xaa₍₁₆₎Xaa₍₁₇₎GluGly (SEQ ID NO:33), wherein Xaa₍₆₋₇₎ is two amino acids.
37. The peptide of claim 31 wherein Xaa₍₅₎ is Arg.
38. The peptide of claim 31 wherein Xaa₍₆₋₇₎ is absent or is AlaGly.
39. The peptide of claim 31 wherein Xaa₍₁₁₎ is Trp.
40. The peptide of claim 31 wherein Xaa₍₁₄₎ is Glu.
41. The peptide of claim 31 wherein Xaa₍₁₅₎ is Lys.
42. The peptide of claim 31 wherein Xaa₍₁₆₎ is Tyr.
43. The peptide of claim 31 wherein Xaa₍₁₇₎ is Phe.
44. The peptide of claim 31 comprising one of the following

sequences: ArgAlaGlyProLeuGluTrpLeuAlaGluLysTyrGluGly (SEQ ID NO:34); ArgProLeuGluTrpLeuAlaGluLysTyrPheGlu (SEQ ID NO:35); or ArgAlaGlyProLeuGluTrpLeuAlaGluLysTyrPheGlu (SEQ ID NO:36).

45. The peptide of claim 1 that contains 10-60 amino acids.

46. The peptide of claim 31 that contains 10-60 amino acids.

47. A composition comprising the peptide of claim 1 in a carrier.

48. The composition of claim 47 further comprising a growth hormone, a growth hormone releasing peptide, a growth hormone releasing hormone, a growth hormone secretagogue, an IGF, an IGF in combination with an IGF binding protein, an IGF binding protein, growth hormone in combination with growth hormone binding protein, insulin, or a hypoglycemic agent.

49. The composition of claim 47 suitable for inhalation.

50. A method for increasing serum and tissue levels of biologically active IGF-I in a mammal comprising administering to the mammal an effective amount of the composition of claim 47.

51. A kit comprising a container containing the composition of claim 47 and instructions directing the user to utilize the composition.

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